International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article.

Prognostic Factors in Head and Neck Non-Hodgkin's Lymphoma (NHL) with Special Reference to Serum Lactate Dehydrogenase (LDH) Levels

Gopika Kalsotra[1], Anchal Gupta[2*], Arun Manhas[3], Rupali Sharma[3]

[1]MS (ENT), Assistant Professor, [2]MS (ENT), Lecturer, [3]MBBS, Post Graduate Student,
Department of Otorhinolaryngology, SMGS Hospital, Government Medical College, Jammu, J&K- UT, India.

ABSTRACT

Introduction: The head and neck region is the second most frequent anatomical site of extranodal lymphomas. These tumours affect many individuals worldwide, justifying epidemiological studies in different countries. This present study evaluated the characteristics, treatments and prognostic factors for non-Hodgkin's lymphoma of the head and neck in our institute.

Materials and Methods: The clinical manifestations, clinicopathological characteristics, site of primary lesion, histopathological diagnosis, staging, multidisciplinary treatment and prognostic factors which includes age, sex, general condition at the time of diagnosis, presence of bulky disease, mediastinal involvement, extranodal site involvement, immunophenotype and serum lactate dehydrogenase (LDH) level for 75 patients with non-Hodgkin's lymphoma of the head and neck were analysed retrospectively.

Results: Male: female ratio of 1.08: 1 was seen. The most common site was Waldeyer's ring. About three-fourth patients presented at Stage I and Stage II of disease. Overall survival rate (3 yrs) was 60%.Younger age group(<20 yrs) had poor prognosis than adults(>20 yrs). Females had better prognosis than males. Waldeyer's ring and nasal cavity NHL had poor survival rate (<50%) than PNS, larynx, trachea & others (>75%). Serum LDH values (>250 U/L) were higher in patients with stage III and stage IV of the disease as compared to stage I and stage II. 3year survival rate became poorer as stage advanced.

Conclusion: The knowledge of prognostic factors helps in early diagnosis and adequate treatment. Advanced age and stage, males, a particular site (Waldeyer's ring), intermediate and high-grade type, serum LDH levels, radiotherapy/chemotherapy alone were various factors which may worsen the prognosis and survival pattern in NHL of head and neck region.

Keywords: Lymphomas, Prognosis, Serum Lactate Dehydrogenase.

***Correspondence to:**

Dr. Anchal Gupta, MS (ENT),
Lecturer, Department of Otorhinolaryngology,
SMGS Hospital, Government Medical College,
Jammu, Jammu and Kashmir UT, India.

Article History:

Received: 16-04-2021, **Revised:** 08-05-2021, **Accepted:** 29-05-2021

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2021.7.3.015	

INTRODUCTION

Malignant lymphomas are a diverse group of malignancies arising from the lymphoreticular system. malignant lymphoma. NHL comprises approximately 5% of head and neck. Hodgkin's and non- Hodgkin's lymphomas can be found in the head and neck region; but extranodal disease, with or without lymph node involvement, is more common among NHL patients.[1]

They constitute the third most common neoplasm in the head and neck region after squamous cell carcinoma and salivary gland tumors.[2] Hodgkin's disease and non-Hodgkin's lymphoma (NHL) are the two main types of malignancies and displays a wide range of appearances comparable with Hodgkin's disease.[3] Lymphoma of the head and neck presenting as an unknown mass has often proven to be a challenge for diagnosis.[4] When lymphoma cannot be easily differentiated from carcinoma, it often leads to multiple biopsies, diagnostic delays, occasional large anatomical dissections to obtain adequate tissue, and even inadvertent ablative procedures. Lymphomas has a propensity to involve atypical extranodal head and neck and central nervous system (CNS) sites.[5] NHL is treated mainly with radiotherapy and/or chemotherapy. Lactate dehydrogenase (LDH) is a glycolytic enzyme that may be elevated in the serum of patient's with NHL. Serum LDH has been found to be significantly correlated both to the spread of the disease and to the histological grade of malignancy i.e. more advanced disease or more aggressive histopathology is associated with higher serum LDH values.[6] Our retrospective study aims to identify patient characteristics, sites of involvement, treatment response and survival rate and to describe the important prognostic factors for patients including age, sex,

general condition at the time of diagnosis, presence of bulky disease, mediastinal involvement, extranodal site involvement, immunophenotype and serum lactate dehydrogenase (LDH) level.

MATERIALS AND METHODS

A retrospective review was made of all cases of non-Hodgkin's lymphomas involving the head and neck at the ENT outpatient department of our institute betweenJanuary 2013 and January 2019. Specifically, the clinical presentations, site of primary lesion, histological diagnosis, staging, and prognostic factors for NHL with head and neck involvement were sought. The disease was clinically staged at the time of diagnosis according to Ann Arbor Staging system using parameters of physical examination, X-ray chest, computed tomography, blood counts, biochemistry (particularly serum LDH levels), UGI series, bone marrow aspiration. Data was also reviewed for treatment modality, overall survival and duration of follow up.

Statistical Analysis: Statistical Analysis was performed by applying IBM SPSS statistics for windows version 25.0 (IBM Corp. Released 2017, Armonk, NY, USA). Categorical variables were represented in the form of number and percentage while continuous variable as mean ± standard deviation.

OBSERVATIONS AND RESULTS

Age and Sex Distribution of Patients

The present study included 75 patients of NHL of head and neck with the age range 8-90 years (median age 48.7 ± 10 years) and male: female ratio of 1.08: 1 (39 males and 36 females). Figure 1 shows genderwise distribution of patients.

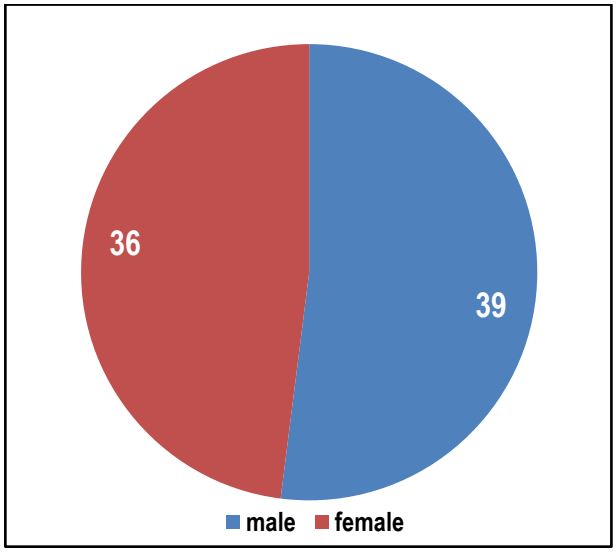

Figure 1: Genderwise distribution of patients

Sites of Lesion

The most common site of involvement was Waldeyer's ring seen in 53(70.6%) patients. Out of these, 30(40%) patients had involvement of palatine tonsils, 11(14.6%) patients showed nasopharyngeal involvement and 12(16%) patients had base of tongue involvement. The next common site of involvement was paranasal sinuses seen in 7(9.3%). Nodal involvement by NHL was seen in 6(8.3%) patients. 4(5.3%) patients had oral cavity NHL. 2(2.6%) patients each showed involvement of nasal cavity and larynx whereas only 1(1.3%) patient showed tracheal involvement. Figure 2 shows distribution of patients according to site of lesion.

Stage at Presentation

According to Ann Arbor staging, 25(33.3%) patients presented at stage I, 30(40%) patients presented at stage II, 10(13.3%) patients presented at stage III and 10(13.3%) patients presented at stage IV of disease.

Histological Grading of NHL

Based on histology NHL was classified as low grade in 9(12%) patients, intermediate grade in 54(72%) patients and high grade in 12(16%) patients.

High Grade Malignancy (n = 12)

- Immunoblastic B (n = 5) or T (n = 1)
- Lymphoblastic B (n = 4) or T (n = 2)

Intermediate Grade Malignancy (n = 54)

- Centroblastic (n = 36)
- Centroblastic/ Centrocytic diffuse (n = 7)
- Centrocytic diffuse (n = 5)
- Lymphoplasmacytoid pleomorphic (n = 6)

Low Grade Malignancy (n = 9)

- Centoblastic/ Centrocytic follicular and follicular and diffuse (n = 6)
- Lymphoplasmacytic and Lymphoplasmacytoid (n = 3)

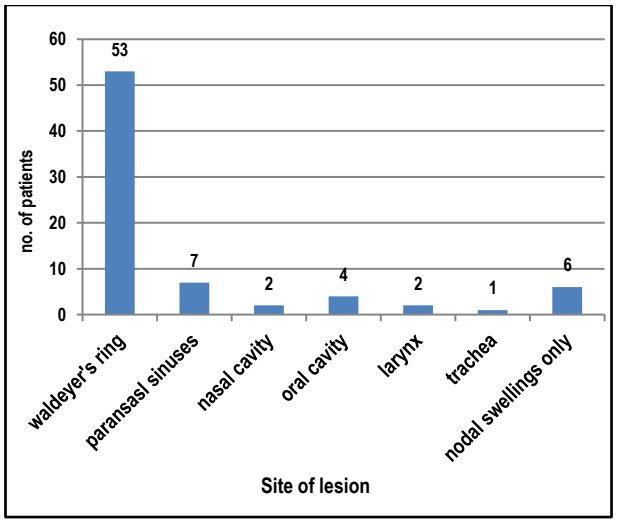

Figure 2: Distribution of patients according to site of lesion

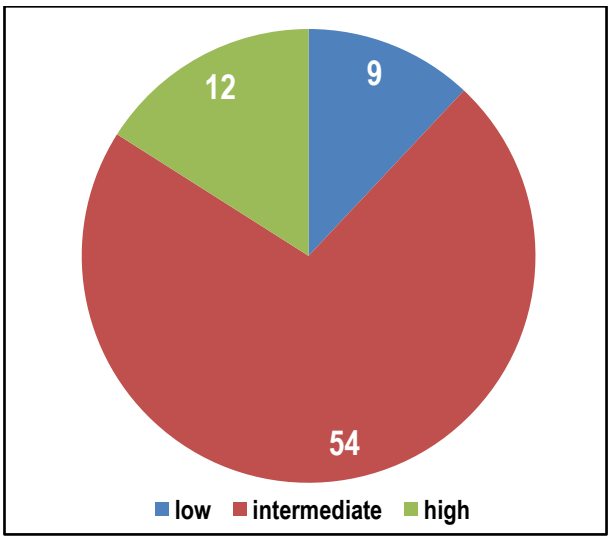

Fig 3: Distribution according to histological grading.

Among 75 patients who were studied at diagnosis, raised serum LDH (>250 U/L) levels were seen in 20(26.6%) patients and among these patients a high LDH value was seen in 8/12 (66.6%) of the patients with high grade, whereas in intermediate grade 12/54 (22.2%) showed elevated serum LDH levels. Incidentally out of 9 patients with low grade subtype of lymphoma, none of the patient showed raised serum LDH levels in our study.

Table 2 shows relationship of high serum LDH to stage of disease and several presenting features among patients with high grade and intermediate grade lymphoma. General symptoms including fever and bulky disease were associated to high serum LDH especially in patients with high and intermediate grade lymphoma.

Symptoms at Presentation

16(21.33%) patients presented with constitutional symptoms like weight loss, fever and pruritis. The extranodal involvement was seen in 63(84%) patients. The nodal involvement was seen in 6(8.3%) patients. The extranodal involvement with lymph node metastasis was seen in 41(54.6%) patients. The NHL was seen as second malignancy in 4(5.3%) patients. The presenting symptoms varied according to the site of lesion. Follow up period ranged from 6 months to 3 years. Table 2 shows that high serum LDH levels was seen in patients with bulky disease (16 of 34 patients,47%), marrow involvement (15 of 20 patients,75%), splenomegaly (13 of 13 patients, 100%), mediastinal tumor (11 of 12 patients, 91.6%), liver involvement (12 of 30 patients,40%) and leukemic syndrome (5 of 6 patients, 83.3%). It was hence observed that high serum LDH values are more frequent in high grade and intermediate grade lymphomas. High serum LDH is also associated with bulky disease, big mediastinal mass, splenomegaly, bone marrow involvement, liver involvement and leukemic syndrome. Stage III (5 of 6 patients, 83.3%) and stage IV (9 of 10 patients,90%) showed high serum LDH levels. In stage I disease no patient (0 of 22) showed high serum LDH levels whereas in stage II only 6 of 28 (21.4%) showed high serum LDH levels.

Treatment and Outcome

Chemotherapy was the mainstay of treatment but radiation was used along with for bulky disease only. Chemotherapy alone was used as treatment modality in 42 (56%) patients. Radiation along with chemotherapy was used in 33 (44%) patients. Drug regimen used was CHOP (cyclophosphamide, Adriamycin, Oncovin, Prednisone) as it was affordable & tolerable. Table I shows treatment modalities in various stages of tumor.

Prognostic Factors and the Survival Pattern

Overall survival rate (3 years) was 60%. With respect to age, no statistical difference was found in 3 year survival between any two decades but younger age group (<20 yrs) (30%) had poor prognosis than adults (>20 yrs) (59%). Females (72%) had better prognosis than males (42%) (P<0.001). Waldeyer's ring and Nasal cavity NHL had poor survival rate (<50%) than PNS, larynx, trachea & others (>75%). 3year survival rate became poorer as the stage advanced.

Table 1: Relationship of raised serum LDH levels (> 250U/L) to Lymphoma subtypes in patients at the time of diagnosis

SUBTYPE	Raised serum LDH levels (> 250 U/L) (n)	%
High Grade	8/12	66.6%
Intermediate Grade	12/54	22.2%
Low Grade	0/9	0%

Table 2: Number of cases with raised LDH > 250 U/L/Total number of cases with high and intermediate grade malignancy non-Hodgkin Lymphoma who were studied at diagnosis, before starting any treatment

Parameters		Raised serum LDH >250 U/L		
		High Grade	**Intermediate Grade**	**Total**
Stage I		0/1	0/21	0/22
Stage II		1/2	5/26	6/28
Stage III		2/3	3/3	5/6
Stage IV		5/6	4/4	9/10
General symptoms	**(No)**	3/5	1/26	4/31
	(Yes)	5/7	11/28	16/35
1. Bulky Disease	**(No)**	2/5	2/27	4/32
	(Yes)	6/7	10/27	16/34
2. Marrow Involvement	**(No)**	2/6	3/40	5/46
	(Yes)	6/6	9/14	15/20
3. Splenomegaly	**(No)**	5/9	2/44	7/53
	(Yes)	3/3	10/10	13/13
4. Mediastinal tumor	**(No)**	5/8	4/46	9/54
	(Yes)	3/4	8/8	11/12
5. Liver involvement	**(No)**	5/8	3/28	8/36
	(Yes)	3/4	9/26	12/30
6. Leukemic Syndrome	**(No)**	8/12	7/48	15/60
	(Yes)	0/0	5/6	5/6

Table 3: Showing treatment modalities in various stages of disease.

Stage	Radiotherapy	Chemotherapy	Radiotherapy + chemotherapy
I	-	12	7
II	-	8	17
III	-	10	9
IV	-	12	-
Total	-	42(56%)	33(44%)

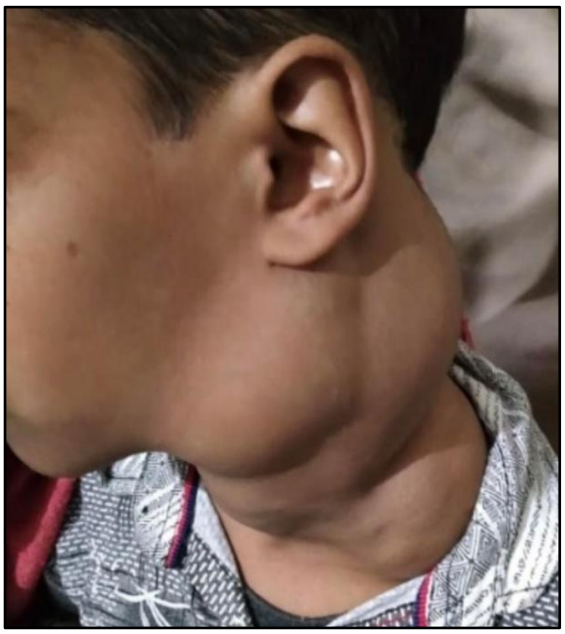

Figure 4: Picture showing NHL of neck in a 14 year old boy.

DISCUSSION

NHL consists of various subtypes with different natural histories and therapeutic responses. This malignancy can be ominous in the head and neck region due to the multiplicity of vital structures.[7] Nodal disease usually appears as a non-tender mass or a number of masses while the extranodal form may be mistaken for more common conditions such as squamous cell carcinoma, thyroiditis, anaplastic carcinoma or metastasis from an unknown primary.[8]

According to the results obtained in our study, the mean age of the patients of NHL was48.7 $\pm$ 10 years, which was lower than that described in a number of studies that found a mean age of approximately 60 years for NHL of head and neck patients.[7,9] The mean age of individuals with extranodal NHL in the present study was also roughly similar to that described in previous investigations.[10,11]

In contrast to previous studies[7,9], a male predilection was seen in our study with male: female ratio of 1.08:1. Several factors including genetic and environmental discrepancies may be responsible for the differences detected between these reports.

Waldayer's ring has been reported as a common site of primary extranodal NHL in the head and neck, with the tonsils being the most prevalent tissue of involvement.[12]

Various studies showed extranodal NHL mainly in Waldayer's ring (32%), especially the tonsils.[8-10] In our study also, the most common site of involvement was Waldeyer's ring seen in 53 (70.6%) patients. Out of these 30 (40%) patients had involvement of palatine tonsil, 11 (14.6%) patients showed nasopharyngeal involvement and 12(16%) patients had base of tongue involvement.

Correlation between histologic grading and primary site of involvement was found in our series. Majority of NHL in Waldeyer's ring & nasal cavity were of intermediate or high grade lesions in agreement with study by Shimm et al.[12] Kapadia SB[13] in his study stated –high grade lesions are most common in nasopharynx and rest (thyroid, larynx, trachea) were of low grade.

Nathu et al.[14] reported that sex of the patient did not affect the prognosis and Conley et al.[8] showed that survival of patients with low grade NHL was better than intermediate & high grade. In our study also, females had significantly better prognosis and low grade NHL had a better outcome.

Fasola G et al.[15] in their study found that high serum LDH values were more frequent in high grade lymphomas than intermediate grade lymphomas and were rare in low grade subtypes. Hagberg and Siegbahn[6] in their study confirmed that serum LDH was higher in stages III and IV than in stages I and II by using the classification of Lennert.[16]

Fasola G et al.[15] also found out that high serum LDH values were always associated with at least two or more other disease features which includes general symptoms, bulky disease, a big mediastinal mass, liver involvement, splenomegaly, bone marrow involvement and leukemic syndrome, which was also seen in our study.[17-20]

Also stage I & II pts had good prognosis and advanced staged pts had poor prognosis found in accordance with previous reports. Jacob & Hoppe[21] in their study stated that prognosis in NHL is influenced by primary site and noticed poor prognosis for NHL of PNS(5 yr survival 12%)(bulky disease, unfavourable histology & local Radiotherapy alone) but our cases had good prognosis for the same (3 yr survival 75%) (intermediate grade, combined Radiotherapy and chemotherapy)

Traditionally, stage I& II disease are treated by radiotherapy alone initially. Combined Radiotherapy and chemotherapy are superior to radiotherapy alone with respect to overall survival, disease and relapse free survival.

We found that stage I & II patients tended to have better 3 year survival (65%) with combined chemotherapy and radiotherapy although difference was not statistically significant. Cabanillas et al.[22] and Miller and Jones[23] found chemo alone effective for stage I& II disease. Cabanillas et al.[22] recommended radiotherapy followed by chemotherapy in stage II patients with bulky disease. In our study 3year survival for 6 patients of stage II treated by chemo alone was excellent.

CONCLUSION

Advanced age and stage, males, a particular site (Waldeyer's ring), intermediate and high-grade subtype of NHL, high serum LDH levels are various prognostic factors in NHL of head and neck region. Serum LDH might be useful both as a prognostic marker and to monitor the course of the disease.

REFERENCES

1. Hanna E, Wanamaker J, Adelstein D, Tubbs R, Lavertu P. Extranodal lymphomas of the head and neck. A 20-year experience. Arch Otolaryngol Head Neck Surg 1997: 123: 1318–23.
2. Kolokotronis A, Konstantinou N, Christakis I,et al.Localized B-cell non-Hodgkin's lymphoma of oral cavity and maxillofacial region: a clinical study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005: 99: 303–10.
3. King AD, Lei KI, Richards PS, Ahuja AT. Non-Hodgkin's lymphoma of the nasopharynx: CT and MR imaging. Clin Radiol 2003: 58: 621–5.
4. Hanto DW, Frizzera G, Gajl-Peczalska KJ. Epstein-Barr virus–induced B-cell lymphoma after renal transplantation: acyclovir therapy and transition from polyclonal to monoclonal B-cell proliferation. N Engl J Med 1982; 306:913–8.
5. Finn DG. Lymphoma of the head and neck and acquired immunodeficiency syndrome: clinical investigation and immunohistological study. Laryngoscope 1995; 105 (Suppl 68): 1–18.
6. Hagberg H, Siegbahn A. Prognostic value of serum lactic dehydrogenase in non-Hodgkin's lymphoma. Scand. J. Haematol 1983; 31: 49-56.
7. Neville BW, Damm DD, Allen CM, Bouquot JE. Oral and maxillofacial pathology. Philadelphia: WB Saunders Co. 2008.
8. Conley SF, Staszak C, Clamon GH, Maves MD. Non-Hodgkin's lymphoma of the head and neck: the University of Iowa experience. Laryngoscope 1987: 97: 291–300.
9. Dubey SP, Sengupta SK, Kaleh LK, Morewaya JT. Adult head and neck lymphomas in Papua New Guinea: a retrospective study of 70 cases. Aust N Z J Surg 1999: 69: 778–81.
10. Urquhart A, Berg R. Hodgkin's and non-Hodgkin's lymphoma of the head and neck. Laryngoscope 2001: 111: 1565–9.
11. Economopoulos T, Asprou N, Stathakis N, et al. Primary extranodal non-Hodgkin's lymphoma of the head and neck. Oncology 1992: 49:484–8.
12. Shimm DS, Dosoretz DE, Harris NL, Pilch BZ, Linggood RM, Wang CC. Radiation therapy of Waldeyer's ring lymphoma. Cancer 1984;54:426–31.
13. Kapadia SB. Hematologic diseases. In: Barnes L, ed. Surgical Pathology of the Head Neck, ed 2. New York: Marcel Dekker, 2001:1045–209.
14. Nathu R, Mendenhall N, Almasri N, Lynch JW. Non-Hodgkin's lymphoma of the head and neck: a 30-year experience at the University of Florida. Head Neck 1999;21:247–54.
15. Fasola G, Fanin R, Gherlinzoni F. Serum LDH concentration in non-Hodgkin's lymphomas. Relationship to histologic type, tumor mass, and presentation features. Acta Haematol 1984; 72: 231–8.
16. Lennert K. Histopathology of non-Hodgkin's lymphoma (based on the Kiel classification) Springer, Berlin (1981).
17. Ciampi A, Bush RS, Gospodarowicz M, Till JE. An approach to classifying prognostic factors related to survival experience for non-Hodgkin's lymphoma patients: based on a series of 982 patients: 1967-1975. Cancer 1981; 47: 621-7.
18. Herrmann R, Barcos M, Stutzman L,et al. The influence of histologic type on the incidence and duration of response in non-Hodgkin's lymphoma. Cancer 1982; 49: 314-22.
19. Horwich A, Peckham M. 'Bad risk' non-Hodgkin's lymphomas. Semin. Hematol. 1983; 20: 35-56.
20. Portlock CS. 'Good risk' non-Hodgkin's lymphomas: approaches to management. Semin. Hematol. 1983; 20: 25-34.
21. Jacobs C, Hoppe RT. Non-Hodgkin's lymphomas of head and neck extranodal sites. Int J Radiat Oncol Biol Phys 1985; 11: 357–64.
22. Cabanillas F, Body G, Freireich E. Management with chemotherapy only of stage I and II malignant lymphoma of aggressive histologic types. Cancer 1980; 46: 2356–9.
23. Miller TP, Jones SE. Initial chemotherapy for clinically localized lymphomas of unfavorable histology. Blood 1983; 62: 413–8.

Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: Gopika Kalsotra, Anchal Gupta, Arun Manhas, Rupali Sharma. Prognostic Factors in Head and Neck Non-Hodgkin's Lymphoma (NHL) with Special Reference to Serum Lactate Dehydrogenase (LDH) Levels. Int J Med Res Prof. 2021 May; 7(3): 58-62. DOI:10.21276/ijmrp.2021.7.3.015